

CLAIMS

We claim:

1. A method of screening for bioactive agents capable of inhibiting an IL-4 inducible ϵ promoter, said method comprising

a) combining a candidate bioactive agent and a cell comprising a fusion nucleic acid comprising:

i) an IL-4 inducible ϵ promoter; and

ii) a reporter gene;

b) inducing said promoter with IL-4; and

c) detecting the presence or absence of said reporter protein;

wherein the absence of said reporter protein indicates that said agent inhibits said IL-4 inducible ϵ promoter.

2. A method according to claim 1, wherein said reporter gene encodes a fluorescent protein.

3. A method according to claim 1, wherein said reporter gene encodes a death protein that is activated by the introduction of a ligand, and said method further comprises adding said ligand to said cell.

4. A method according to claim 3, wherein said fusion nucleic acid further comprises a different reporter gene.

5. A method according to claim 3 wherein said death protein is a Fas receptor and said ligand is Fas.

6. A method according to claim 5 wherein said Fas receptor is a chimeric receptor comprising:

a) the extracellular domain of murine Fas receptor; and

b) the cytosolic domain of human Fas receptor.

7. A method according to claim 3 wherein said death protein is a chimeric protein comprising:

- a) the extracellular domain of a ligand-activated dimerizing receptor; and
- b) the cytosolic domain of a Fas receptor.

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8. A method according to claim 7 wherein said ligand-activated dimerizing receptor is selected from the group consisting of CD8 receptor, erythropoietin receptor, thrombopoietin receptor, growth hormone receptor, Fas receptor, platelet derived growth hormone receptor, epidermal growth factor receptor, leptin receptor, an interleukin receptor, low-density lipoprotein receptor, prolactin receptor, and transferrin receptor.

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9. A method according to claim 1 wherein said fusion nucleic acid comprises an exogenous IL-4 inducible ϵ promoter.

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10. A method according to claim 1 wherein said fusion nucleic acid comprises an endogenous IL-4 inducible ϵ promoter.

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11. A method according to claim 1 wherein said combining is done by introducing a retroviral vector comprising nucleic acid encoding said candidate bioactive agent to said cell.

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12. A method according to claim 11 wherein a library of retroviral vectors comprising a library of candidate bioactive agents is added to a population of cells.

13. A method according to claim 11 wherein said retroviral vector further comprises nucleic acid encoding a fluorescent label.

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14. A method according to claim 2 or 13 wherein said detecting is done using a FACS machine.

15. A cell line for screening selected from the group consisting of CA-46 and MC-116, said cell line comprising a fusion nucleic acid comprising:

- a) an IL-4 inducible ϵ promoter; and
- b) a reporter gene.

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16. A method of screening for bioactive agents capable of modulating IgE production, said method comprising:

- a) combining a candidate bioactive agent and a cell capable of expressing IgE;
- b) determining the amount of IgE produced in said cell;

wherein a change in the amount of IgE as compared to the amount produced in the absence of said candidate agent indicates that said agent modulates IgE production.

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17. A method according to claim 16 wherein said modulation is a decrease in the amount of IgE.

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18. A method according to claim 16 wherein said cell comprises a IgE fusion protein comprising:

- a) the ϵ heavy chain; and
- b) a fluorescent protein.

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19. A method according to claim 16 wherein said combining is done by introducing a retroviral vector comprising nucleic acid encoding said candidate bioactive agent to said cell.

20. A method according to claim 19 wherein a library of retroviral vectors comprising a library of candidate bioactive agents is added to a population of cells.

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21. A method according to claim 19 wherein said retroviral vector further comprises nucleic acid encoding a fluorescent label.

22. A method according to claim 16 wherein said detecting is done by the addition of a fluorescent antibody against IgE.

23. A method of screening for bioactive agents capable of inhibiting a promoter of interest,
5 said method comprising

a) combining a candidate bioactive agent and a cell comprising a fusion nucleic acid comprising:

i) a promoter of interest; and

10 ii) a reporter gene comprising a death gene that is activated by the introduction of a ligand;

b) optionally inducing said promoter;

c) introducing said ligand to said cell; and

15 d) detecting the presence of said cell, wherein the presence of said cell indicates that said agent inhibits said promoter.

24. A method according to claim 23 wherein said fusion nucleic acid further comprises a different reporter gene.

25. A method according to claim 23 wherein said promoter is an endogenous promoter.

26. A method according to claim 23 wherein said promoter is an exogenous promoter.

27. A composition comprising:

a) a test vector comprising:

25 i) a first selection gene;

ii) a fusion gene comprising:

1) a first sequence encoding a transcriptional activation domain; and

2) a second sequence encoding a test protein; and

b) a reporter vector comprising:

30 i) a first detectable gene;

ii) all or part of the switch ϵ sequence, which upon binding of said transcriptional activation domain due to a protein-nucleic acid interaction between said test protein and said switch ϵ sequence, will activate transcription of said first detectable gene.

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28. A method of identifying proteins that bind to all or part of the switch ϵ region of Figure 2B, said method comprising:

- a) providing a host cell comprising the composition of claim 27;
- b) subjecting said host cell to conditions under which the fusion gene is expressed to produce a fusion protein; and
- c) determining whether a protein-nucleic acid interaction between said fusion protein and said switch ϵ sequence occurred.

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